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| 09/518,165 | 03/01/2000 | Vladimir Andrei Koulchin | | 4746 |

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DATE MAILED: 06/03/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/518,165 | KOULCHIN ET AL. | |
| | Examiner | Art Unit | |
| | Ja-Na A Hines | 1645 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *11 March 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *22-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

### *Amendment Entry*

1. The amendment filed March 11, 2002 has been entered. Claims 3-11 and 15-21 have been cancelled. Claims 22-52 have been newly added, thus claims 22-52 are under consideration in the office action.

### *Drawings*

2. The drawing corrections will not be held in abeyance. Applicant must submit proposed drawing corrections in response to the requirement in the Office action.

### *Priority*

3. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, the provisional application upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 22-52 of this application. 09/518,165 is drawn to a method of detecting the presence of a carbohydrate antigen characteristic of at least one species or serogroup of both gram negative and gram-positive bacteria. However, none of the parent applications, for which priority is claimed 09/139,720, 09/156,486, 09/397,110 and 09/458,998 teach a method for detecting both gram-negative and gram-positive bacteria and associated devices. The specification, at pages 2-6 recite incorporating by reference the individual aspects of each application, i.e., using essentially free carbohydrate antigens from particular species such as *Legionella* and *S. pnuemoniae*, however there is no teaching of a method wherein both gram-negative and gram-positive bacteria are assayed for. There was no conception of

a generic method to detect the presence or concentration of any bacterial species, but rather to only detect specific species of bacteria such as Legionella or *S. pnuemoniae.* Thus, priority cannot be granted to 09/139,720, 09/156,486, 09/397,110 and 09/458,998 since what is now claimed, has not been previously recited in the other applications.

***Specification***

4. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details. The language should be clear and concise and should not repeat information given in the title.

5. The attempt to incorporate subject matter into this application by reference to 09/156,486, 09/397,110 and 09/139,720 on page 2; 09/458,988 on page 4; 07/706,639 on page 9 and the like as recited throughout the instant specification is improper because a mere reference to another application, is not an incorporation since the documents do not appear to be published. However, if the applications have been published, the patent number needs to entered in place of the serial number.

6. The disclosure is objected to because of the following informalities: Page 2 paragraph 3 refers to Legionella species as Gram-positive, however Legionella are Gram-negative bacteria. Appropriate correction is required.

***Claim Objections***

7. Claim 22 is objected to because of the following informalities: Claim 22 misspells "serogroup" as "serogruop" in line 2 of claim 22. Claim 22 (e) recites by contact of the liquid sample as opposed to contacting the liquid sample. Appropriate correction is required.

8. Claims 45-46 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 43 is drawn to a specific bacterium, Legionella. Claims 45 and 46 broaden, rather than narrow the scope of the invention.

9. The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

There are two claims numbered 43. Therefore the first misnumbered claim 43 has been renumbered 42 pursuant to rule 1.126.

***Withdrawal of Rejections***

10. The following rejections have been withdrawn:

a) The rejection of claims 11, 18 and 21 under 35 U.S.C. 112, second paragraph;

b) the rejection of claims 11 and 21 under 35 U.S.C. 103(a) as being unpatentable over Imrich et al. (US Patent 5,415,994) in view of Cuatrecasas et al. (US Patent 4,411,832); and

c) the rejection of claim 18 under 35 U.S.C. 103(a) as being unpatentable over of Imrich et al.(US Patent 5,415,994) in view of Cuatrecasas et al. (US Patent 4,411,832) in further view of Yen et al. (US Patent 4,206,094) and Hansen et al., (5,356,778).

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 22-52 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is an enablement rejection.

Claims 22 is drawn to a method for detecting the presence of a carbohydrate antigen while claim 43 is drawn to an ICT device, wherein both comprise culturing a bacterial species, obtaining from a wet cell pellet essentially protein free carbohydrate antigen, coupling a spacer molecules to the essentially protein-free carbohydrate

antigen, passing antibodies to produce purified carbohydrate antigen specific antibodies and conducting an assay. However the instant specification fails to provide any experiments that show the combination of purifying the carbohydrate antigen and conducting an assay as one method for detecting the presence of a carbohydrate antigen. Rather the specification teaches, starting at page 14, teach separate steps for the purification of carbohydrate antigen of *Haemophilus influenzae* in example 2, preparation of affinity columns in example 3; purification of *H. influenzae* antibodies in example 4 and ICT assay for *Haemophilus influenzae* type b in example 5. The art purification is highly unpredictable and the instant specification fails to provide any information that any one of the bacterial carbohydrate antigens could be purified and detected in the claimed manner. There is no teaching of a method for detection that encompasses combining all the separate examples into one hybrid method. Moreover, there appears to be no conception of a method for detecting the presence of a carbohydrate antigen characteristic of at least one species or serogroup of a species of bacteria, i.e., both gram negative and gram positive bacteria in one method using one purification procedure for any type of bacteria.

There is merely a general outline of purifying carbohydrate antigens and elucidating antibodies which bind, however the outline is not specific to different types of bacteria. There is no teaching of a wet cell pellet in specification; separating the mixtures into two layers, and separating the layers; or removing the upper layer or how to achieve such. There is teaching in the specification for using a broad-spectrum protease. There is support for separating out an essentially protein free carbohydrate

antigen. Moreover, there is no support for obtaining an essentially protein free carbohydrate antigen by a series of substeps now claimed. The specification at page 14 teaches different purification of carbohydrate antigen steps, including an incubation step, sonication step, repeated precipitation and centrifugation steps, lyophilization, subjected to Lowry assay for proteins and tested for carbohydrate by phenol-sulfuric acid method. The instant claims do not recite any of these method steps. There appears to be no support in the specification for obtaining an essentially protein-free carbohydrate antigen in the manner now claimed. Furthermore, the claims are not enabled for conducting as assay by contacting liquid sample with a detection agent which essentially comprises labeled purified antigen-specific antibodies.

Currently the claims do not requires a particular type of bacteria; and in view of the method for detection of any type of bacteria, the specification fails to teach how to produce a purified antigen specific antibody that binds to an essentially protein free carbohydrate bacterial antigen. In order to achieve the functional limitation of an essentially protein-free carbohydrate antigen and purified antigen specific antibodies, the disclosure needs to teach purification procedures specific to individual species of gram negative and gram positive bacteria, or prove that any bacteria can be purified by the same generic methods. The disclosure does not teach how to achieve the instantly claimed property or assurance of particular results which would be obtained if certain direction were pursued (Critical Synergy: The Biotechnology Industry and Intellectual Property Protection, Presentation of the intellectual Property Committee of the Biotechnology Industry Organization at the October 17, 1994, Hearing of the U.S.

Patent and trademark Office, San Diego, CA, published by the Biotechnology Industry Organization, Washington, D.C. pages 100-107). Producing an essentially protein free carbohydrate bacterial antigen is a highly empirical process yet the specification fails to teach the critical or key characteristics of the bacterial carbohydrate antigens; moreover, the specification needs to teach particular combination of reagents. There are an infinite number of combinations of possible columns, gradients, gels, centrifugations, in combination with appropriate buffers of varying pH, salt, etc., however, the specification is not enabled for obtaining from the wet cell pellet an essentially protein-free carbohydrate antigen from any bacteria by a series of substeps, thus the claim should be so limited. In absence of further guidance from applicants as to how to purify the antigens to a degree which is an essentially protein-free carbohydrate antigen, and in view of the unpredictability and complexity in the art, it would require undue experimentation on the part of a skilled artisan to discover the key and critical characteristics of the bacteria which allow one skilled in the art to choose from the plethora of bacterial purification procedures in order to achieved an essentially protein-free carbohydrate antigen.

The claims are further drawn to conducting an assay which comprising detecting crude carbohydrate antigen of a species of bacteria by contacting the liquid sample with a detection agent which essentially comprises labeled purified antigen-specific antibodies, however the specification recites, at page 20 section C, Immunoassay procedures, require adding "reagent A", Tween 20, sodium azide, sodium dodecydl sulfate in sodium citrate phosphate buffer to produce the crude carbohydrate antigen,

however the instant claims fail to recite adding the appropriate reagents. Moreover, the specification does not appear to enable the use of any bacteria with the recited reagents especially when Legionella is extracted a different "reagent A" solution (tris base containing SB3-8, a zwitterionic detergent) See 09/458,998 page 9. Thus, it is unclear that one of skill in the art could follow these general guidelines and achieve purification of an essentially protein-free carbohydrate antigen.

Claim 24 recites derivative of either lipoteichoic acid or teichoic acid however, there appears to be no support in the specification for the derivatives of either, thus the claims are not enabled for derivatives of either acid. The specification provides no guidance as to what derivatives of either lipoteichoic acid or teichoic acid are. The claims broadly recite said derivatives, but fails to disclose the production of specific derivatives of the acids. Thus the recitation of derivative of either lipoteichoic acid or teichoic acid is not enabled by the specification. The substitution of any derivative would not predictably result in a detectable crude antigen. The specification does not provide guidance on how to produce said derivatives from the crude antigen. No working examples are shown containing the missing information. Without such information, one of skill in the art could not predict which derivatives of the acids will enable the detection of the crude antigen in the recited method. Accordingly, one of skill in the art would be required to perform undue experimentation to use derivatives of either lipoteichoic acid or teichoic acid to detect the crude antigen. Therefore, one skilled in the art could not make and/or use the invention without undue experimentation.

The instant claims, 43-52, are not limited to the O-linked carbohydrate antigens, but rather to essentially free protein carbohydrate antigens. However application 09/139,720 teaches detailed preparation of antibodies specific to O-carbohydrate antibodies of *Legionella pneumophila*. The specification of 09/458,998 on page 4 at line 10-12 states that " applicants the developed a modified enzyme immunoassay ("EIA") using a coated tube in which *L. pneumophila* serogroup 1 raw polyclonal antibodies that have been purified according to the affinity purification procedure described and claimed in the parent application." See also page 5 paragraph 1 of the 09/458,998 specification. Therefore, the purified raw polyclonal antibodies and procedures disclosed in both 09/139,720 and 09/458,998 specification are what is being used in the instant application when referring to Legionella. Therefore, the claims of the instant application, need to claim the same O-carbohydrate antigens and purified raw polyclonal antibodies as described in the specifications. Claims 43-52 of the instant application fail to require the use the O-polysaccharide antigen sample or the use of purified raw polyclonal antibodies. Claims 43-52 of the instant application are not commensurate in scope with the examples taught in the specifications of 09/139,720 or 09/458,998. The 09/139,720 specification requires conjugation and coupling of the O-polysaccharide antigen to the chromatographic column and further requires affinity purification of the antibodies to the O-polysaccharide antigen. The O-polysaccharide antigen must be present to create the antigen specific *Legionella* antibodies. Thus purified raw polyclonal antibodies recognizing the O-carbohydrate antigen of *Legionella* will bind and detect the presence

of *Legionella*. However, the claims of the instant application do not recite the essential use of the O-carbohydrate antigen or their purified raw polyclonal antibodies. Therefore, the claims do not include the limitations taught by the parent specification, thus they are not enabled.

Claims 36 and 45 recite esters of either lipoteichoic acid or teichoic acid, however the there appears to be no support for the ester of either in the specification, thus the claims are not enabled for esters of either acid. The specification provides no guidance as to what esters of either lipoteichoic acid or teichoic acid can be produced. The claims broadly recite said esters, but fails to disclose the production of specific esters. Thus the recitation of esters of either lipoteichoic acid or teichoic acid is not enabled by the specification. The substitution of any esters would not predictably result in a detectable crude antigen. The specification does not provide guidance on how to produce esters from the crude antigen. No working examples are shown containing the missing information. Without such information, one of skill in the art could not predict which esters of the acid will enable the detection of the crude antigen in the recited method and device. Accordingly, one of skill in the art would be required to perform undue experimentation to use esters of either lipoteichoic acid or teichoic acid to detect the crude antigen. Therefore, one skilled in the art could not make and/or use the invention without undue experimentation.

Absent clear demonstration of the detection of any bacterial carbohydrate antigen, the purification and detection methods could not used in any well-established

manner. In absence of further guidance from applicants, the skilled artisan would have to discover what the appropriate substrate is and the conditions under which each gram negative and/or gram-positive bacteria could be extracted. Such experimentation requires ingenuity beyond that expected of one of ordinary skill in the art. Such need for none routine experimentation demonstrates the specification is not enabled for the asserted use or well-established use for detection of bacterial carbohydrate antigens. Accordingly, the specification is not enabled for using the alleged method and device in any manner disclosed.

12. Claims 22-52 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 22-52 are drawn to a method for detecting the presence of a carbohydrate antigen characteristic of at least one species or serogroup of a species of bacteria in a fluid comprising culturing an identified species as a wet cell pellet, obtaining from a well cell pellet essentially protein free carbohydrate antigen, as recited in claim 22(a) (b) and (b)(i). There is no teaching of a well cell pellet in specification. In claim 22 (b)(iii)(iv), the claim recites separating the mixtures into two layers, and separating the layers, however there is no support in the specification for separating the mixture or removing the upper layer. There is no support for the use of a broad-

spectrum protease. There is support for separating out an essentially protein free carbohydrate antigen as recited in claim 22 (b)(vii). Moreover, the there is no support for obtaining an essentially protein free carbohydrate antigen by a series of substeps now claimed. The specification at page 14 teaches different purification of carbohydrate antigen steps. There appears to be no support in the specification for the hybrid claims drawn to obtaining an essentially protein-free carbohydrate antigens and conducting as assay by contacting liquid sample with a detection agent which essentially comprises labeled purified antigen-specific antibodies. See also, claim 43, which recites the same steps and lacks support for such steps. Claim 24 recites derivative of either lipoteichoic acid and teichoic acid however, the appears to be no support in the specification for the derivatives of either; claim 37 and 46 recites esters of either lipoteichoic acid and teichoic acid, however the there appears to be no support for the ester of either in the specification. Claims 33 and 42 are drawn to detecting *Haemophilus influenzae* type b, however there appears to be no support in the specification for using the claimed purification steps to specifically purify Haemophilus antigen. Applicant has not pointed to support in the specification by page and line number. Thus, the amendment introduces new matter.

13. Claims 22-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The terms "strong acid" " approximate neutrality" " broad spectrum protease enzyme" "weakly alkaline" "essentially protein free" in claim 22 are relative terms which render the claim indefinite. The terms are not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention.

Claim 22 is unclear. Claim 22 (d) it is unclear because it recites passing antibodies over the chromatographic affinity gel to produce purified carbohydrate specific antibodies, however it is unclear where the antibodies came from. There is no recitation by the claim as to making the antibodies, thus the antibodies must be obtained before they are passed through the column. Clarification is requested.

Claim 22 (d) and (e) recite the limitation "purified antigen-specific antibodies", however here is insufficient antecedent basis for this limitation in the claim. The claim should recite purified carbohydrate antigen-specific antibodies.

Also, it is suggested that the last word of claim 22 "hereof" be deleted from the claim.

Claim 22 recites the limitation "the crude antigen component thereof". There is insufficient antecedent basis for this limitation in the claims.

14. Claim 24 recites derivative of either (lipoteichoic acid or teichoic acid). The specification is silent concerning a definition of what constitutes the metes and bounds of such derivatives of either lipoteichoic acid or teichoic acid. Therefore, the claim is unclear and indefinite as to what is encompassed by the phrase "derivative of either". It is unclear how to define the derivative when there appears to be no support in the

specification for the derivatives of either. Thus the metes and bounds of the claim cannot be ascertained.

15. Claim 36 and 45 recites esters of either (lipoteichoic acid and teichoic acid) however this recitation makes the claim indefinite. The specification is silent concerning a definition of what constitutes the metes and bounds of such derivatives of either lipoteichoic acid or teichoic acid. Therefore, the claim is unclear and indefinite as to what is encompassed by the phrase "derivative of either". It is unclear how to define the derivative when there appears to be no support in the specification for the derivatives of either. Thus the metes and bounds of the claim cannot be ascertained.

16. Claim 35-36 and 44-45 are incorrect. Gram-positive bacteria can be detected by their lipoteichoic acid, and teichoic acid, while its lipopolycarbohydrate antigen can detect gram-negative bacteria; gram negative or positive bacteria are not detected by the antigens listed in claims 35-36 and 44-45.

17. Dependant claims 44,46 are not commensurate in scope with independent claim 43 and are therefore unclear. Claim 43 is drawn to using essentially protein free carbohydrate antigen obtained from a culture of Legionella, which is a gram bacterium, however claims 44 and 46 are drawn to using Gram-positive bacteria. Thus the claims attempt to broaden the scope of the claims. Thus it is unclear how the ICT device of claim 43 which is drawn to using antigen of Legionella can further incorporate gram-positive antigens.

***Incorporation By Reference***

18. The incorporation of essential material in the specification by reference to another patent application is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973). US application 09/139,720 and 09/458,998 describe the purification of an essentially protein free lipo-carbohydrate antigen of bacteria of *Legionella* species, while 09/39,110 describes the purification proves to an essentially protein-free state of the C-polysaccharide cell wall antigen present in *S. pneumoniae* serotypes. Thus each reference is attempting to incorporate essential purification procedures. The attempt to incorporate subject matter into this application by references to 09/139,720, 09/397,110 and 09/458,998 are improper because the incorporation by reference attempts to incorporate essential material.

***Double Patenting***

19. Claims 22-32, 34-40, and 43-51 of this application conflict with claims 10-14 and 25-29 of Application No. 09/458,998. Claims 22, 26-32, 34-40, and 43-51 of this application conflict with claims 33-36, 41, 43-45, and 50-54 of Application No. 09/397,110. 37 CFR 1.78(b) provides that when two or more applications filed by the

same applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one application. Applicant is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP § 822.

20. Claims 22-23, and 25 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 10-14 and 25-29 of copending Application No. 09/458,998. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims in 09/458,998 are drawn to a method of determining the concentration of at least one species or serogroup of *Legionella* bacteria in water comprising the recited steps. 09/458,998 is drawn to a method of determining the concentration of *Legionella* bacteria in a fluid/water sample comprising: culturing a *Legionella* species, obtaining from a wet cell pellet essentially protein free carbohydrate antigen, coupling a spacer molecules to the essentially protein-free carbohydrate antigen, passing antibodies and conducting an assay. While 09/518,165 is drawn to a method of detecting the presence of at least one group or serogroup of bacteria in a fluid sample comprising the same steps as recited 09/458,998. The method of determining the concentration of the *Legionella* in application of 09/458,998 is inherently encompassed by the detection of the bacteria 09/518,165 when the same method steps are recited. Therefore 09/458,998 is not patentably distinct from 09/518,165.

21. Claims 22, 24, 26-32, 34-40, and 43-51 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 33-36, 41, 43-46, and 50-54 of copending Application No. 09/397,110. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims in 09/518,165 are drawn to a method of determining the presence of a carbohydrate antigen of at least one species or serogroup of bacteria comprising the recited steps: culturing an identified species, obtaining from a wet cell pellet essentially protein free carbohydrate antigen, coupling a spacer molecules to the essentially protein-free carbohydrate antigen, passing antibodies and conducting an assay. While 09/139,720 is drawn to a method of detecting the presence of at least one group or serogroup of *Streptococcus pneumoniae* bacteria in a fluid sample comprising: culturing a *Streptococcus pneumoniae* species, obtaining from a well cell pellet essentially protein free carbohydrate antigen, coupling a spacer molecules to the essentially protein-free carbohydrate antigen, passing antibodies and conducting an assay which are the same recited steps. The method of determining the presence of *Streptococcus pneumoniae* (09/397,110) is inherently encompassed by the detection of the carbohydrate antigen of bacteria as recited by 09/518,165 when the same method steps are recited. Thus 09/139,720 is not patentably distinct from 09/518,165.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

**New Grounds for Rejection**
***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

22. Claims 43-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Imrich et al., (US Patent 5,415,994) in view of Barthe (J. Clin. Micro. 1988).

Imrich et al. (US Patent 5,415,994), teach devices, methods and kits for detecting analytes in biological sample where prior to detection, extraction can occur (col.1 lines 5-10). Clinical detection of microbial pathogen in biological samples can determine accurately and rapidly infectious pathogens (col. 1 lines 23-30 and col. 7 lines 2). Biological material can be obtained from patients and includes urine, serum, sputum, and pharyngeal exudates (col.3 lines 9-13). Non-patient non-biological samples may also be used (col. 3 lines 25-28). The device comprises a labeling zone having means for specifically labeling the analyte or first zone and a capture zone or second zone (col.3 lines 48-56). Bibulous materials such as untreated paper, nitrocellulose, derivatized nylon, cellulose (col. 4 lines 56-63). The matrix comprises at least two zones, and the matrix defines a lateral flow path (Col. 4 lines 64-68). The labeling zone contains a means for specifically labeling the target analyte. The labeling means will generally be a labeled immunoglobulin such as an antibody (col. 5 lines 15-23). The label may be soluble or particulate and may include dyed immunoglobulins binding substances such as dyes, polymers, latex beads or metallic sols (col. 5 lines 28-38). Imrich et al., incorporates by reference US Patent 4,373,932 which teaches the use of

metallic gold sol. As sample flows through the labeling zone, the target analyte in the sample binds the labeled antibody thereby indirectly labeling the target analyte. The sample continues to flow into the capture zone on the matrix. As the sample flows into the capture zone, labeled target analyte will bind the immobilized immunoglobulins thereby retaining label in the capture zone. The presence of analyte in the sample may then be determined by visual identification of label retention in the capture zone (col. 5 lines 50-52). The device has an observation window located over the capture zone of the matrix (col. 7 lines 10-20). The device can simultaneously detect many different analytes such as *Legionella pneumophila*, and *Haemophilus influenzae* (col. 7 lines 1-5). However, Imrich et al., does not specifically teach using antibodies which detect crude carbohydrate antigens.

Barthe et al., teach a common epitope on the lipopolysaccharide of *Legionella* pneumophila recognized by a monoclonal antibody. One monoclonal antibody produced attached to a common epitope from eight serogroups of *Legionella* (page 1016). The materials and methods teach production of the monoclonal antibodies, preparation of outer membrane, and immunoassay detection. Table 1 shows detection of different strains of Legionella in an ELISA assay format. Carbohydrate antigens are defined in the instant specification as including lipopolysaccharides (page 9).

Claims 42-46 are drawn to an ICT device, whiles claims 48-52 are drawn to a method of detection using the device, however the claims recite the use of antigen-specific antibodies. The claims are drawn to a product by process, however the process for creating an essentially free protein carbohydrate antigen do not create provide for a

materially different antibody. The antibody of Barthe et al., will also bind to the crude carbohydrate antigen. Thus, absent evidence to the contrary, the antibody of Barthe et al., meets the limitations of the claimed device, by being capable of binding to crude carbohydrate antigens. Moreover, there are no structural difference between the claimed antibody and device and the antibody and device of the recited prior art. A structural difference needs to exist in order to patentably distinguish the claimed invention from the prior art; the prior art antibody and device are capable of performing just like the instantly claimed device, thus they meet the claimed limitations.

No more then routine skill is involved in adjusting the amount of component of the claimed process to suit a particular concentration. Changes in concentrations do not impart patentability unless recited in ranges which produce new and unexpected results. *In re Aller et al.* (CCPA 1955) 220 F2d 454, 105 USPQ 233. Therefore, the recitation that the antibodies are present in a concentration of between 7.7 nanograms per square millimeter and 35 nanograms/square millimeter of surface area in both the first and second zones does not describe a patentable difference, neither would the recited concentration achieve unexpected results.

It would have been prima facie obvious to modify the immunochromatographic device for the detection of an antigen of a species of bacteria, which comprises a first and second zone and method for detecting the crude antigen as taught by Imrich et al., to include the monoclonal antibody of Barthe et al., because Barthe et al., antibody recognizes several crude carbohydrate antigens from *Legionella*. One would have a reasonable expectation of success by incorporating the an antibody with recognizes a

common epitope found on Legionella, into the device and method of Imrich who already teach using the antibodies to bind and label the bacterial antigens to detect there presence. Moreover, no more then routine skill would have been required to use an alternative yet functionally equivalent antibody in the labeling and capturing technique of Imrich et al., since only the expected results would have been obtained; thus the use of alternative and functionally equivalent techniques would have been desirable to those of ordinary skill in the art based on the monoclonal antibodies ability to recognize several *Legionella* serogroups.

***Response to Arguments***

23. Applicants assert that Imrich et al., does not suggest any assay process in which purified antibodies are employed for the purpose of improving sensitivity and specificity of the assay but speaks only of immunoglobulin apparently on the premise that any immunoglobulin from any source will do.

However, applicants claims are drawn to device, thus the source of immunoglobulins also known as antibodies, do not provide a structural difference between the device of Imrich et al., in view of Barth et al., as recited above. A structural difference between the claimed invention and the prior art needs to exist in order to patentably distinguish the claimed invention from the prior art; the prior art device is capable of performing just like the instantly claimed device, therefore it meets the limitations of the claims.

Applicants claims drawn to a method for detection require contacting the liquid sample with the strip of bibulous material of the ICT device; allowing lateral flow from the first zone to the second zone and observing a color change which indicates the presence of bacteria. The method claims do not limit the source of antibodies, therefore the antibodies of Imrich et al., in view of Barthe et al., satisfy the claim limitations.

Applicants assert that Imrich contain no suggestion that it would be helpful to combine an assay with affinity purification of the antibodies to be used in the assay, however, there are no structural differences between the antibodies of Imrich et al., in view of Barthe et al., and the instantly claimed antibodies. The antibodies of the recited prior art can bind to the crude antigen just as the instantly recited antibodies can. Moreover, there is no evidence to the contrary that the antibodies of the prior art will not bind to the crude antigen. It is noted that the claims use a product produced by a particular process. It is noted that the patentability of a method relying on a product does not depend on the method of production of that product. In re Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985). Similarly to extend, the process used to produce the product that is claimed (i.e., product by process), does not confer a patentable difference upon the product used in the assay nor does it distinguish it from native protein in the prior art. Since the Patent Office does not have the facilities for examining and comparing applicants' antibody with the antibody of the prior art reference, the burden is upon the applicants to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the antibody of the prior art does not possess the same material structural and functional characteristics of the claimed antibody). See In

re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicant's arguments with respect to Cuatrecasas et al., Yen et al., and Hansen et al., have been considered but are moot in view of the new ground(s) of rejection.

24. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

25. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na A Hines whose telephone number is

703-305-0487. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 703-308-3909. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Ja-Na Hines JH
May 28, 2002

Pat a. Duffy
PATRICIA A. DUFFY
PRIMARY EXAMINER